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EXAMINER

KERR, KATHLEEN M

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 12/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/916,045	Applicant(s) SANTI ET AL.	
	Examiner Kathleen M Kerr	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 September 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7 and 12-26 is/are pending in the application.
- 4a) Of the above claim(s) 12-16 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 6 and 7 is/are allowed.
- 6) ☒ Claim(s) 1-4 and 19-26 is/are rejected.
- 7) ☒ Claim(s) 5, 17 and 18 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. A request for continued examination under 37 C.F.R. § 1.114, including the fee set forth in 37 C.F.R. § 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R. § 1.114, and the fee set forth in 37 C.F.R. § 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 C.F.R. § 1.114. Applicant's submission filed on September 23, 2004 has been entered.

Application Status

2. In response to the previous Office action, a Final rejection (mailed on June 1, 2004), Applicants filed a response and amendment received on September 23, 2004. Said amendment amended Claims 5*, 6, 7 and added new Claims 17-26. Thus, Claims 1-7 and 12-26 are pending in the instant Office action.

3. The Examiner notes that Claim 5 has been amended, although it is not appropriately marked in the version filed by Applicant on September 23, 2004 (see claims filed February 12, 2004).

Election

4. Claims 1-7 and 12-26 are pending in the instant application. Claims 12-16 are withdrawn from consideration as non-elected invention(s); said claims are not subject to rejoinder since the elected group is drawn to method claims. Thus, Claims 1-7 and 17-26 will be examined herein.

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Priority

5. As previously noted, the instant application is granted the benefit of priority for the U.S. Provisional Application No. 60/220,651 filed on July 25, 2000.

Withdrawn - Objections to the Specification

6. Previous objection to the specification for the following discrepancy is withdrawn by virtue of Applicant's amendment.

Withdrawn - Claim Objections

7. Previous objection to Claims 6 and 7 for depending from a rejected claim is withdrawn by virtue of Applicant's amendment rendering the instant claims independent.

Withdrawn - Claim Rejections - 35 U.S.C. § 112

8. Previous rejection of Claim 5 under 35 U.S.C. § 112, first paragraph, written description, is withdrawn by virtue of Applicant's amendment (although not noted on the claim set filed September 23, 2004) limiting the claim to using exactly metyrapone.

Maintained - Claim Rejections - 35 U.S.C. § 112

9. Previous rejection of Claims 1-4 under 35 U.S.C. § 112, first paragraph, written description, is maintained. Moreover, Claims Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons.

Applicant reiterates arguments concerning operativeness vs. written description of the previously set forth rejection. The Examiner maintains that the written description rejection and subsequent analysis of record is proper. Written description has a basis in how the disclosed

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species (single or multiple) describe(s) (support(s)) the claimed genus. In the instant case, a single species is exemplified. That is, while several species are described because such experiments are considered, only a single species is reduced to practice (while Applicant need not reduce to practice all of their embodiments, the specification must adequately describe the claimed genus). This exemplification was cited to assist in Applicant's understanding that the species (singular) disclosed does not adequately describe the claimed genus. Applicant is correct, though, that other species are disclosed. This mere disclosure of a genus and naming of several species within that genus does not necessarily mean that written description is adequate for said genus; consider *Enzo Biochemical* (63 USPQ2D 1609, CAFC 2002) wherein "we do not agree" "that the written description requirement for the generic claims is necessarily met as a matter of law because the claim language appears *in ipisis verbis* in the specification." Further, the "disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described", thus it is not enough to know the function of the claimed genus without some correlating structure so that the skilled artisan can "visualize or recognize the identity of the subject matter". For these reasons, the sum total of these species (plural) also does not adequately describe the claimed genus.

Inasmuch as Applicant "reiterated the arguments made in the previous response"; the Examiner reiterates the previous response to applicant's arguments. Applicant then continues argument in a section title "Allowability of New Claims 19-22", in which previous rejections are referenced, thus the Examiner must assume that these are more arguments of the same vein and they will be addressed herein.

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Applicant argues that an assay of epoK activity is described and P450 inhibitors are “of the well known nature”. Applicant further notes issues of nature of the invention, guidance provided by the specification, and knowledge of one of [ordinary] skill in the art - all of which are issues of enablement, which while considered for a written description rejection under the statute 35 U.S.C. § 112, are not the standard.

Applicant argues that “P450 inhibitor” and “epoK gene product inhibitor” “are not new or unknown biological materials that ordinarily skill artisans would readily miscomprehend” (emphasis in original) and thus, *U. Cal v. Lily* and *Enzo Biochemical* are inapposite to the instant case (Applicant cites *Amgen*) as cited by the Examiner previously. The Examiner disagrees. *Amgen* describes *Lily* (not *U. Cal. v. Lily*) and *Enzo* as inapposite to the *Amgen* facts. *Amgen* is concerned the description of with cells types that can be used to produce recombinant human erythropoietin wherein cell types are well known in the art (as indicated by the opinions in *Amgen*) in the art; *Lily* and *Enzo* are cases with new or unknown biological materials. Thus, the claims in the instant claims must not be considered in light of *Amgen* (description of well known cell types) but in light of *Lily* and *Enzo* (description of “not new and unknown biological materials”) for the following reasons.

Firstly, the Examiner disagrees that epoK-gene-product-inhibitors are well known in the art. No examples are described in the art save this patent application.

Secondly, the Examiner disagrees that the subset of P450 inhibitors that inhibit epoK is well known in the art for congruent reasons.

Applicant contrasts (a) the fact that Claim 7 is considered to have adequate written description, wherein said claim lists six P450 inhibitors professed by the instant specification to

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inhibit epoK and be useful in the claimed invention, and (b) the fact that the genus of P450 inhibitors that inhibit epoK lacks adequate written description (new claim 19). The Examiner will herein clarify the Office's position. In Claim 7, the P450 inhibitors listed in the methods are not a genus, they are each species. Since a genus is not in the claimed methods, the analysis under 35 U.S.C. § 112 is one of clarity (2nd paragraph) and enablement (1st paragraph, previously addressed in prosecution) because the individual species are supported in the specification as originally filed - not by reduction to practice but by clear envisioning such that one of skill in the art would understand that Applicant was in possession of methods using these six inhibitor compounds. This is in contrast to claiming use of the genus of P450 inhibitors that inhibit epoK; this genus is a subset of P450 inhibitors having a specific function. In this case, the genus must be adequately described by correlated structure and function. This is where the specification lacks adequate written description for the claimed genus of methods.

Applicant then continues argument in a section title "Allowability of New Claims 23-26". Applicant argues that P450 inhibitors are well known and, thus, are adequately described as a genus to be used in the claimed methods. While P450 inhibitors are common in the art, they are not as well known as vertebrate cells, as in the case of *Amgen*, so as to arbitrarily disregard their need for adequate written description. As evidenced below in the new rejection of Claims 23-26, P450 inhibitors are "unknown biological materials" (from *Amgen*) inasmuch as the genus of such inhibitors is incomplete and recognized only by function since no common structural features are described in the art or the specification (see for example, Halpert JR. Structural Basis of Selective Cytochrome P450 Inhibition. Annual Review of Pharmacology and Toxicology (1995) 35:29-53). With this in mind, the assessment in *Enzo Biochemical* requiring (1) a representative

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species and (2) a correlation of structure and function between the representative species and the claimed genus, applies.

NEW ISSUES

Claim Objections

10. Claims 5, 17, and 18 are objected to as depending from a rejected claim.
11. Claims 5 and 17 is objected to under 37 C.F.R. § 1.75 as being a substantial duplicate of claim 6. When two (or three) claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See M.P.E.P. § 706.03(k).
12. Claim 18 is objected to under 37 C.F.R. § 1.75 as being a substantial duplicate of claim 7. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See M.P.E.P. § 706.03(k).

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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13. Claims 19-26 are rejected under 35 U.S.C. § 112, first paragraph, written description, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant claims are drawn to methods using reversible P450 enzyme inhibitors, optionally a subset of said inhibitors that reduce the activity of epoK; said claims lack adequate written description for both P450 enzyme inhibitors and the subset of which also reduce the activity of epoK.

The Court of Appeals for the Federal Circuit has recently held that a “written description of an invention involving a chemical genus, like a description of a chemical species, ‘requires a precise definition, such as be structure, formula [or] chemical name,’ of the claimed subject matter sufficient to distinguish it from other materials.” *University of California v. Eli Lilly and Co.*, 1997 U.S. App. LEXIS 18221, at *23, quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these (see *Enzo Biochemical*, 63 USPQ2D 1609, CAFC 2002).

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University of Rochester v. G.D. Searle & Co. (69 USPQ2d 1886 (2004)) specifically points to the applicability of both *Lily* and *Enzo Biochemical* to methods of using products, wherein said products lack adequate written description. While in *University of Rochester v. G.D. Searle & Co.* the methods were held to lack written description because not a single example of the product used in the claimed methods was described, the same analysis applies wherein the product, used in the claimed methods, must have adequate written description as noted from *Enzo Biochemical* (see above).

In the instant specification, a single example of an epothilone epoxidase inhibitor useful in the claimed methods is exemplified, using metyrapone (see Example 4); other P450 enzyme inhibitors as postulated as being useful although not reduced to practice. While the specification describes, at length, procedures for assaying for inhibitors of epothilone epoxidase using a purified epoK gene product (pages 20-21) and while the specification proposes numerous compounds as inhibitors, such as P₄₅₀ enzyme inhibitors, acetylenic mechanism-based inhibitors, etc., still only a single species of the inhibitors is exemplified. No discussion of the structure of metyrapone and how that structure relates to inhibiting function is described in the specification. In fact, the structures of the numerous proposed inhibitors and classes of inhibitors do not appear to have structural features in common with metyrapone. Thus, having only a single, exemplified representative species (and having six additional proposed species) and no structure/function relationship of how that species functions to inhibit epoK, the species cannot adequately describe the claimed genus.

Moreover, P450 enzyme inhibitors as a whole lack a common structural feature; these compounds are a genus described only by function. Thus, such a genus clearly fails under the

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test prescribed by *Enzo Biochemical* for adequate written description of products and by

University of Rochester v. Searle wherein said products are used in a claimed method.

Summary of Pending Issues

14. The following is a summary of the issues pending in the instant application:

- a) Claims 5 and 17-18 stands objected to as depending from a rejected claim.
- b) Claims 5, 17 and 18 stand objected to under 37 C.F.R. § 1.75 as being a substantial duplicate of another allowed claim.
- c) Claims 1-4 and 19-26 stand rejected under 35 U.S.C. § 112, first paragraph, written description.

Allowable Subject Matter

15. As previously noted, "Claim 6, drawn to methods of making desoxyepothilone by fermentation in the presence of metyrapone is free of the prior art. No prior disclosure of treatment of epothilone-producing microorganisms with this compound is known. While the prior art teaches inactivating the epoK gene recombinantly to produce an epothilone PKS in the absence of an epoxidase function for production of useful epothilones C and D (see particularly USPN 6,303,342), no motivation for using epoxidase inhibitors instead of recombinantly producing this same effect can be found since recombinant means are easier, less detrimental to the overall growth of the host cell, and described so as to be enabled in the prior art, unlike use of epoxidase inhibitors."

Conclusion

16. Claims 6-7 are allowed. Claims 5, 17, and 18 are objected to and Claims 1-4 and 19-26 are rejected for the reasons identified in the numbered sections of this Office action. Applicants

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must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (571) 272-0931.

The examiner can normally be reached on Monday through Friday, from 9:00am to 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Kathleen M Kerr
Primary Examiner
Art Unit 1652

December 21, 2004